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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/577,688	04/28/2006	Tetsuhiko Yoshida	TESHP103US	9807

23623 7590 03/09/2009

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EXAMINER	
GUPTA, ANISH	
ART UNIT	PAPER NUMBER
1654	

NOTIFICATION DATE	DELIVERY MODE
03/09/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/577,688	YOSHIDA ET AL.	
	Examiner	Art Unit	
	ANISH GUPTA	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 December 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18* is/are pending in the application.

4a) Of the above claim(s) *4, 10-14 and 18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,5-9 and 15-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4-28-06, 10-24-06, 9-24-07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group II, claims 1-3, 5, 6-7, 8-9, 15-17 drawn to peptide having the sequence of SEQ ID NO 10-30, with the elected species of SEQ ID NO 10 in the reply filed on 12-4-08 is acknowledged.

It should be noted that Claim 14 was inadvertently included in with Group II. The restriction requirement was based on the claims corresponding to SEQ ID NO 1-9 and SEQ ID NO 10-30. Claim 14 corresponds to SEQ ID 1-9, which was identified as being part of Group I. Thus, it should have been clear that claim 14 actually corresponded to Group I, rather than Group II. Accordingly, claim 14 has been placed in Group I and Group II is now drawn to 1-3, 5-7, 8-9 and 15-17.

A search was conducted for the elected species of SEQ ID NO 10. This was found to be free of the prior art. The search was extended to SEQ ID NO 11-30 and these peptides were also found to be free of the prior art. Since the claims allows for 6 allows for "one or a plurality of amino acids residue(s) conservatively replaced," the search was extended for conservative substitutions. Prior art was found for SEQ ID NO 11. This art has been applied below. Claims 1-3, 5-7, 8-9 and 15-17 read on the species and have been examined.

Claims 4, 10-14 and 18 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected Groups, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 12-4-08.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1-3, 5, 8 and 15-17 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The MPEP states that the purpose of the written description requirement is to ensure that the inventor had possession, as of the filing date of the application, of the specific subject matter later claimed by him. The courts have stated:

> "To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966." Regents of the University of California v. Eli Lilly & Co., 43 USPQ2d 1398.

The MPEP lists factors that can be used to determine if sufficient evidence of possession has been furnished in the disclosure of the Application. These include "level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention. Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient." MPEP 2163.

Further, for a broad generic claim, the specification must provide adequate written description to identify the genus of the claim. In Regents of the University of California v. Eli Lilly & Co., the court stated:

> "A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials. Fiers, 984 F.2d at 1171, 25 USPQ2d at 1606; In re Smythe, 480 F.2d 1376, 1383, 178 USPQ 279, 284-85 (CCPA 1973) ("In other cases, particularly but not necessarily, chemical cases, where there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated, one skilled in the art may be found not to have been placed in possession of a genus. . . ."). Regents of the University of California v. Eli Lilly & Co., 43 USPQ2d 1398.

The MPEP further states that if a biomolecule is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is "not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." MPEP 2163. The MPEP does state that for generic claim the genus can be adequately described if the disclosure presents a sufficient number of representative species that encompass the genus. MPEP 2163. If the genus has a substantial variance, the disclosure must describe a sufficient variety of species to reflect the variation within that genus. See MPEP 2163. Although the MPEP does not define what constitute a sufficient number of representative, the Courts have indicated what do not constitute a representative number species to adequately describe a broad generic. In Gostelli, the Court determined that the disclosure of two chemical compounds within a subgenus did not describe that subgenus. In re Gostelli, 872 F.2d at 1012, 10 USPQ2d at 1618.

In the instant case, the claims are drawn to artificially designed antimicrobial peptides composed of at least 6 contiguous amino acid residues selected form the an amino acid sequence constituting laminin binding site or a sequence with one or more plurality of amino acid residue(s)

conservatively replaced and an amino acid sequence that can express antimicrobial activity against one kind of bacteria or fungi. This generic statement of description of the antimicrobial peptide does not provide ample written description because the generic statement provide sufficient relavent identifying characteristics. First, the claims do not set forth a complete structure of the antimicrobial peptides. While the claim states that the peptide is composed of six contiguous amino acid residues from the laminin binding site, this does not provide a partial structure. In describing the laminin binding site, the specification states that laminin binding site and found in every kind or organism and is found in proteins that functions as receptors for laminin, which is non-collagen glycoprotein. This description does not provide a partial structure since the lamin binding site has not been defined to have a consensus sequence.

Furthermore, the claim also states that the peptide contains an amino acid sequence that can express antimicrobial activity. This portion of the molecule is solely defined by function alone. The specification states "antimicrobial peptide" is a term referring to amino acid polymer having a plurality of peptide bonds displaying antimicrobial activity against at least one kind of microbe, and is not limited by the number of the amino acid residues constituting the peptide chain. The antimicrobial peptide in this specification also includes oligopeptides having 10 and below amino acid residues or polypeptides containing 10 or more amino acid residues. Here, unless otherwise specified, "amino acid residue" is a term including N-terminal amino acid and C-terminal amino acid of the peptide chain. It is noted that the definition states that the antimicrobial peptides can contain 10 or more amino acids. This does not provide a partial structure since the only underlying feature of the molecule is repeat of amide bonds. It is, however, it is the side chains of the sequence that provide description in the way of partial structure and not the amide bonds.

The molecule, as claimed, is solely defined by functional characteristics. However, the art does not recognize that antimicrobial peptides with lamin binding site is correlated to a particular structure. That is, there is an absence of teaching in the art and the specification that the a known

structure is correlated to the lamin binding site portion (at least six contiguous amino acids) and antimicrobial portion. It must not be forgotten that the MPEP states that if a biomolecule is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is "not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." MPEP 2163.

As stated earlier, the MPEP states that written description for a genus can be achieved by a representative number of species within a broad generic. It is unquestionable claim 1 is a broad generic with respect all possible peptides with varying length up to 100 amino acids. The possible structural variations are limitless to any length with natural and non-naturally occurring amino acids. The claims also allow for conservative replacement within the sequence. Assuming, arguendo, that laminin binding site is known, the claim still does not account for 94 amino acids. Under this assumption the number of different sequences encompassed by the claims include 2.90×10^{39} different combinations. This number is even greater since the claim allows for non-naturally occurring amino acids and since the laminin binding site is undefined within the claims and the specification. While the specification provide some specific sequences, the sequence disclosed have significant homology and are defined by having a partial structure. Most of the peptide have a significant portion that contains arginine/lysine resides. The sequence disclosed do not contain significant variability that accurately reflects the large genus of the broad claims. The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See In re Wilder, 736 F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate."). Accordingly, it is deemed that the specification fails to provide adequate

written description for the genus of the claims and does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the entire scope of the claimed invention. Accordingly, it is deemed that the specification fails to provide adequate written description for the genus of the claims and does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the entire scope of the claimed invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claims 1-3, 5, 6-7, 8-9, 15-17 rejected under 35 U.S.C. 102(b) as being anticipated by Deber et al. (WO03/000277) as evidenced by Sundstrom et al. (US6388056) or Ford et al. (US6426191).

The claims are drawn to antimicrobial peptides.

The reference teaches the sequence KKKKKKAAWAAWAAWAA-NH2 (see page 9 of the reference). The reference states that the peptides have antimicrobial activity and kills pathogenic organisms such as bacteria, virus, fungi, yeast and mycoplasma (see page 9). The peptide is amidated, there by meeting the limitation of claim 8 and 16. This peptide is a conservative variant of SEQ ID 11, RKKKRKVLMWWML.

The instant specification does not define conservative replacement. It is known it the art that in such amino acid sequences, one or more amino acids in the fundamental sequence may preferably be substituted with another amino acid(s), the charge and polarity of which is similar to

that of the native amino acid, i.e., a conservative amino acid substitution, resulting in a silent change. Substitutes for an amino acid within the fundamental polypeptide sequence can be selected from other members of the class to which the naturally occurring amino acid belongs. Amino acids can be divided into the following four groups: (1) acidic amino acids; (2) basic amino acids; (3) neutral polar amino acids; and (4) neutral non-polar amino acids. Representative amino acids within these various groups include, but are not limited to: (1) acidic (negatively charged) amino acids such as aspartic acid and glutamic acid; (2) basic (positively charged) amino acids such as arginine, histidine, and lysine; (3) neutral polar amino acids such as glycine, serine, threonine, cyteine, cystine, tyrosine, asparagine, and glutamine; (4) neutral nonpolar (hydrophobic) amino acids such as alanine, leucine, isoleucine, valine, proline, phenylalanine, tryptophan, and methionine (see col. 0-10 of US 6388056). Similarly it is known that amino acid "substitutions" are the result of replacing one amino acid with another amino acid having similar structural and/or chemical properties, i.e., conservative amino acid replacements. Amino acid substitutions may be made on the basis of similarity in polarity, charge, solubility, hydrophobicity, hydrophilicity, and/or the amphipathic nature of the residues involved. For example, nonpolar (hydrophobic) amino acids include alanine, leucine, isoleucine, valine, proline, phenylalanine, tryptophan, and methionine; polar neutral amino acids include glycine, serine, threonine, cysteine, tyrosine, asparagine, and glutamine; positively charged (basic) amino acids include arginine, lysine, and histidine; and negatively charged (acidic) amino acids include aspartic acid and glutamic acid (see Col. 8, lines 33-52, US6426191)

Thus it is acknowledged that lysine and arginine form a basis for conservative substitutions. Thus, the first and fourth amino acid are conservatively substituted in the prior art sequence with lysine (replacing arginine). It is also acknowledge, due their nonpolar (hydrophobic) nature, that alanine, valine, leucine methionine and tryptophan form the basis for conservative substations.

Thus, the prior art peptide has conservative a substitution in position 7 (alanine for valine), position 8, 13 (alanine for leucine), position 9, 12 (tryptophan for methionine), and position 10-11 (alanine for tryptophan). Thus, the reference meets the limitation of the claims by disclosing a peptide with "a plurality of amino acid residues conservatively replaced."

4. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anish Gupta whose telephone number is (571)272-0965. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang, can normally be reached on (571) 272-0562. The fax phone number of this group is (571)-273-8300.

/Anish Gupta/
Primary Examiner, Art Unit 1654